shown a closer correlation in across-shift decline in lung function with log cotton dust levels than with log endotoxin levels or the number of gram negative bacteria.

Cloutier and colleagues (1984) noted that many of the hypothesized mechanisms of byssinosis, including bacterial endotoxin effects (Rylander et al. 1979, 1985; Rylander 1981, 1982), nonallergic histamine release (Bouhuys and Lindell 1961; Ainsworth et al. 1979; Noweir et al. 1984), and airways smooth muscle contraction by a 5-hydroxytryptamine (5-HT), receptor agonist (Russell et al. 1982), require that the byssinotic agent cross the airway epithelium. Normally the respiratory epithelium bars inhaled substances from access to the interstitium, to airway smooth muscle, or to the bloodstream (Cloutier et al. 1984). The application of aqueous cotton bract extract to canine trachea has been found to disrupt this barrier by inhibition of transepithelial ion flux (Cloutier et al. 1984). Alteration in the active ion transport may result in an altered osmotic balance in the airway. Although the components of cotton bract extract responsible for the altered ion flux are unknown, Cloutier and colleagues (1984) consider tannin and 5-HT to be likely causes, endotoxin to be a possible cause, and histamine to be an unlikely cause. Other components of the cotton bract, including lacinilene C-7 methyl ether, have also been mentioned as possible etiologic agents (Kilburn 1980).

Inhalation of cigarette smoke can also induce alteration of active ion transport by the airway epithelium (Welsh and Karp 1983). Inhalation of the smoke from one cigarette decreased the electrical potential difference across the tracheal epithelium owing to an inhibition of the rate of chloride ion secretion. Active ion transport by the airway epithelium plays an important role in the regulation of the volume and composition of the respiratory tract fluid. Inhibition of transepithelial ion flux by cotton dust (Cloutier et al. 1984) and by cigarette smoke (Welsh and Karp 1983; Kennedy et al. 1984) may produce the symptoms of acute bronchitis, and each could conceivably have an additive effect upon the other.

Alteration of the osmolarity and the ion concentration of inhaled aerosols can produce both cough and bronchoconstriction (Eschenbacher et al. 1984). These investigators found that in asthmatics, the stimuli for cough could be distinguished from those for bronchoconstriction. They suggest that afferent airway nerve depolarization may occur as a result of anion flux imbalance (outward anionic flux cannot be balanced owing to the inhibition of inward anion movement) and that cough is the reflex response (Eschenbacher et al. 1984). Alternatively, Hogg and Eggleston (1984), noting that disruption of epithelial tight junctions has resulted from transtracheal osmotic gradients, propose a mechanism whereby the vagal irritant reflex receptors located close to the tight junction might be

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deformed by this osmotic disruption. In addition, epithelial injury and sensory receptor sensitization account for increased susceptibility to cough following airways irritation in asthmatic subjects (Empey et al. 1976). It is possible that acute bronchitis in cotton workers may be caused, in part, by similar mechanisms.

Airways Constriction

Cotton dust exposure may induce airways narrowing in atopic individuals (Jones et al. 1980; Parkes 1982). Skin test atopy identifies those at risk of acute bronchoconstriction (cross-shift FEV_1 change) following exposure to high concentrations of cotton dust (elevated levels of both total and respirable dust) (Jones et al. 1980). These results do not necessarily imply that a specific immunoglobulin E (IgE) response is triggered or that elevated levels of IgE (beyond those found in atopic individuals) must be detected in serum (Pepys et al. 1973). The cotton dust bronchoconstrictor response seen in atopics may be nonspecific. Agents extracted from cotton dust have been documented to produce lung injury and physiologic response in previously unexposed volunteers. The presence of an airways response in individuals not previously exposed suggests a pharmacologic or irritant mechanism rather than an idiosyncratic (allergic) one (Buck and Bouhuys 1981; Wegman et al. 1983; Douglas et al. 1984; Haglind and Rylander 1984; Schachter et al. 1985). The nonimmunologic character of the cotton dust lung response is supported by the failure to find precipitating antibodies in the sera of cotton textile workers to extracts of cotton bract, carpels, stems, leaves, cotton lint, or card room cotton dust (Kutz et al. 1981).

Release of bronchoconstricting mediators from the mast cells beneath the bronchial epithelium does not require development of immune hypersensitivity (Dosman et al. 1981; Findlay et al. 1981). The nonspecific reaction induced by cotton dust contrasts with the specific hypersensitivity reactions due to inhaled organic dusts such as complete allergens, e.g., grain dust (Dosman 1977); incomplete haptens, e.g., penicillin (Davies et al. 1974); simple but very reactive copolymerizing compounds, e.g., isocyanate (Butcher et al. 1977); or wood dusts (Chan-Yeung et al. 1973). These specific hypersensitivity reactions are found in relatively few of the exposed individuals, even after a suitable period of exposure (Dosman et al. 1981), and atopy is not required for mediator release (Lam et al. 1979; Bryant and Burns 1976; Boushey et al. 1980).

Nonspecific hyperreactivity may be acquired as a result of chronic exposure to inhaled occupational irritants (Lam et al. 1979). One mechanism for triggering mast cell degranulation and subsequent smooth muscle contraction may result from PGF release from macrophages activated by cotton dust. An aqueous extract of cotton plant "trash" has caused in vitro elaboration of prostaglandins (PGF,

PGE, and PGA) from rabbit alveolar macrophages (Fowler et al. 1981). Bronchoconstriction also may result from changes in airway osmolarity through stimulation of airway mast cells (Findlay et al. 1981) or vagal afferents (Empey et al. 1976; Orehek et al. 1976; Golden et al. 1978; Boushey 1982).

Epithelial injury similar to that observed following a viral upper respiratory infection might expose and stimulate the rapidly adapting sensory receptors of the airway and result in reflex (vagal) bronchoconstriction (Empey et al. 1976). The rapidly adapting sensory receptors extending between the airway epithelial mucosal cells are believed to be involved in ozone-induced hyperreactivity (Golden et al. 1978). Controlled exposures to other agents such as nitrogen dioxide (Orehek et al. 1976) and sulfur dioxide (Boushey 1982) have also resulted in hyperreactivity, possibly owing to vagal sensory fiber stimulation. In addition, byssinosis-like symptoms of cough, chest tightness, substernal soreness, and shortness of breath have been reported by healthy subjects after a controlled 2-hour exposure to ozone at 0.5 to 0.6 ppm (ambient air-pollution concentrations) (Golden et al. 1978). Epithelial injury and sensory receptor sensitization may contribute, therefore, to both cough (bronchitis) and airways constriction (byssinosis).

Barter and Campbell (1976) showed that the rate of deterioration in FEV_1 correlated with methacholine reactivity, independent of the effect of cigarette smoking. Hyperreactivity may therefore indicate the individuals at risk of subsequent loss of function. Although atopic individuals may have an increased susceptibility to bronchoconstriction, at present there is no evidence that atopics are at greater risk of lung disease associated with cotton dust exposure. Perhaps the recent development of an assay for the pharmacologic activity of cotton dust (Douglas et al. 1984) will provide a sufficiently sensitive measure of cotton dust exposure to determine the role of the cholinergic bronchial response in textile workers.

It is possible that the hyperreactivity model for chronic obstructive lung disease may help explain a greater risk of accelerated ventilatory deterioration in cotton textile workers. Van der Lende and colleagues (1970) suggested that airways hyperreactivity might be an underlying factor that led to irreversible obstruction among those exposed to airways irritants. Barter and Campbell (1976) demonstrated an accelerated rate of longitudinal ventilatory function decline in those with hyperreactivity.

Chronic Inflammatory Lung Destruction

Emphysema has been demonstrated post mortem in the lungs of cotton workers (Edwards et al. 1975; Pratt et al. 1980). A significant degree of emphysema, as measured by a reduction of lung elastic

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recoil pressure at total lung capacity, was found only in older (aged 56 to 69) hemp workers (smoking status unspecified) by Guyatt and colleagues (1973). These workers had at least 20 to 30 years of cotton dust exposure. The younger population (aged 31 to 51), studied with a variety of pulmonary function measurements by Zuskin and colleagues (1975), showed no emphysema as documented by normal values of the single breath carbon monoxide diffusing capacity. This finding of emphysematous changes only among older workers is consistent with the data for smokers in the general population, and therefore does not demonstrate a specific effect of cotton dust exposure. Kilburn (1981) reported the prevalence of radiographic changes consistent with emphysema (flattening of the diaphragms and radiolucent or avascular zones of lung) in 233 male cotton textile workers and found that these radiographic changes were present only in the smokers and former smokers in the population.

The data in Tables 8 and 9 are from the study of Pratt and colleagues (1980), who examined fixed, inflated lung specimens from unselected autopsies performed at the Durham (North Carolina) Veterans Administration Medical Center. The findings from the 565 cases with known smoking histories are presented. The mean percentages of centrilobular emphysema (CLE), mucous gland volume, goblet cell metaplasia, and pigmentation grouped by employment or nonemployment as a cotton worker and by smoking status are shown in Table 8. There were 44 cotton workers, 8 of whom were nonsmokers. The statistical results of covariance analyses performed on these data are shown in Table 9. Cotton dust exposure is significantly associated with mucous gland volume and peripheral goblet cell metaplasia in nonsmokers. Cigarette smoking and pipe smoking showed associations with centrilobular emphysema, but no association of emphysema was found with cotton dust exposure. Examination of the main lobar and segmental bronchi showed no morphologic differences between smokers and nonsmokers (Edwards et al. 1984). These data may be interpreted to show that airways inflammation (bronchitis) rather than parenchymal destruction (centrilobular emphysema) follows chronic cotton dust exposure.

Cotton Dust Exposure and Mortality From Respiratory Disease and Lung Cancer

Owing partly to the difficulty in following cohorts of cotton textile workers and partly to the lack of a smoking history among the recorded deaths, there have been few studies of mortality related to cotton dust exposure. In a mortality study of two cohorts of cotton textile workers, Henderson and Enterline (1973) found lower mortality rates overall (SMR 71.7 to 89.6), lower respiratory disease mortality (SMR 36.4 to 76.1) and lower lung cancer mortality (SMR

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TABLE 8.—Mean percentages of centrilobular emphysema, mucus glands, goblet cell metaplasia, and pigmentation

Group	N	Age	Mean percent CLE[1] (all cases)	Mean percent CLE (cases with CLE)	Gland volume (percent)	Goblet cells (percent)	Pigmentation (percent)
All	565	56.2	9.3	24.9	12.1	17.1	5.3
Noncotton	521	56.4	9.2	24.7	12.0	16.7	5.4
Cotton	44	57.6	10.4	26.9	13.0	21.6	4.5
All smokers	460	56.3	11.1	26.4	12.6	18.3	6.3
Smokers (noncotton)	424	56.1	11.0	26.2	12.6	18.0	6.8
Smokers (cotton)	36	57.9	12.6	28.4	12.0	20.4	4.7
Nonsmokers	105	57.3	1.0	6.7	9.8	12.0	2.6
Noncotton	97	57.4	1.1	6.9	9.3	10.7	2.5
Cotton	8	56.5	0.4	3.0	16.3	28.0	3.8
Cigarettes	427	55.6	11.6	26.6	12.6	18.8	6.7
Pipe/cigar	33	65.1	5.6	23.0	12.8	12.2	3.3

[1] CLE = centrilobular emphysema.

SOURCE: Pratt et al. (1980).

TABLE 9.—Covariance model results (F-test probabilities)

Variable	Age	Cigarette smoker	Pipe smoker	Textile exposure	Cigarette textile
			Pipe smokers excluded		
CLE [1]	.002	.0001		NS [2]	NS
Pigment	NS	.0001		NS	NS
Mucus	NS	NS		NS	NS
Goblet	.02	NS		NS	.03
		Cigarette smokers excluded			
CLE	NS		.001	NS	
Pigment	.03		NS	NS	
Mucus	NS		NS	.02	
Goblet	NS		NS	.03	

[1] CLE = centrilobular emphysema.
[2] NS = not significant.
SOURCE: Pratt et al. (1980).

20.5 to 65.3) than expected from the mortality rates of Georgia white men. In a more recent study, Merchant and Ortmeyer (1981) found a doubling of respiratory disease mortality (SMR increased from 61 to 126) with increasing duration of cotton dust exposure from less than 20 to more than 30 years, although no overall mortality excess was observed. Berry and Molyneux (1981) also found no excess mortality associated with cotton dust exposure. Although consistent with previous studies, this last observation must be considered preliminary because less than 10 percent of the Lancashire cotton mill workers under study have died.

Two studies of cancer rates among North Carolina cotton textile employees showed no excess of lung cancer mortality (Heyden and Pratt 1980). Data from the Third National Cancer Survey contain a representative sample of incident cancer cases occurring over 3 years in a population of 21 million men and women who were interviewed to determine their occupation, socioeconomic status, and tobacco and alcohol consumption (Williams et al. 1977). These data indicated a slight (2.06), nonsignificant odds ratio excess risk for lung cancer among male cotton textile workers. While this observation is of interest because the odds ratio was adjusted for smoking, it depended upon only three cases of lung cancer. At this time, therefore, there is no evidence to suggest a lung cancer excess among cotton textile workers.

Control of Cotton Dust Exposure

The feasibility of controlling cotton dust exposure by preprocessing the cotton (heating, washing, or steaming) has been studied by Merchant, Lumsden, Kilburn, Germino, and colleagues (1973).

Although washing the cotton removed detectable biologic effects, the cotton became difficult to spin. Steaming the cotton, while practical for the manufacturer, resulted in an unexpected consequence (Merchant, Lumsden et al. 1974); while it initially removed some of the cotton dust, the steaming process also bound dust to the cotton fiber. Although cotton steaming led to a lower dust level and a smaller fall in cross-shift ventilatory function in the preparation area, subsequent release of the bound dust during spinning resulted in increased dust levels and symptoms of byssinosis and bronchitis in the areas when these processes were performed (Merchant, Lumsden et al. 1974).

The inability to control cotton dust levels by treating the cotton has led to the imposition of Occupational Safety and Health Standards for containment of dust (US DOL 1981). Although these standards have resulted in substantial cost to the cotton textile industry, progress in reducing byssinosis has been made by the implementation of competent air hygiene practices (Kilburn 1983; Gideon and Johnson 1978) using commercially available lint and dust control systems (Barr et al. 1974).

Summary and Conclusions

1. Byssinosis prevalence and severity is increased in cotton textile workers who smoke in comparison with workers who do not smoke.
2. Cigarette smoking seems to facilitate the development of byssinosis in smokers exposed to cotton dust, perhaps by the prior induction of bronchitis. Cotton mill workers of both sexes who smoke have a consistently greater prevalence of bronchitis than nonsmokers.
3. The importance of cigarette smoking to byssinosis prevalence seems to grow with rising dust levels (a smoking–cotton dust interaction). At the highest dust levels, cigarette smoke was found to interact with cotton dust exposure to substantially increase the acute symptom prevalence.
4. Nonsmokers with byssinosis have lower preshift lung function and a greater cross-shift decline in lung function than asymptomatic workers, and those workers with bronchitis generally have lower preshift lung function than those without bronchitis. In general, smokers have lower lung function than nonsmokers among cotton workers, both in those with bronchitis and in those with byssinosis.
5. Although the average forced expiration values measured at the start of a shift are reduced among smokers, the cross-shift decline in function does not seem to be affected by smoking status.

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6. The contribution of the acute byssinotic symptoms (grades 1/2 and 1) to the subsequent development of what have been termed the chronic forms (grade 3) of byssinosis (which include airways obstruction) is not well documented; however, chronic airflow obstruction has been found more frequently in cotton textile workers than in control populations, and this lung function loss appears to be additive to that caused by cigarette smoking.
7. Cotton dust exposure is significantly associated with mucous gland volume and peripheral goblet cell metaplasia in non-smokers, a pathology consistent with bronchitis. Among cigarette smokers, the interaction of cotton textile exposure and smoking is demonstrable for goblet cell hyperplasia. Centrilobular emphysema is found only in association with cigarette smoking and pipe smoking. There is no emphysema association found with cotton dust exposure.
8. The evidence does not currently suggest an excess risk of lung cancer among cotton textile workers.

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CHAPTER 11

IONIZING RADIATION
AND LUNG CANCER

CONTENTS

Introduction

The major focus of this chapter is the interaction of cigarette smoking with radiation exposure; epidemiologic and experimental studies are reviewed. Radon is a noble gas that is created as a consequence of the radioactive decay of radium 226. Its half life is 3.8 days. Radon is of much less health concern than are its immediate decay products (Po-218, Pb-214, Bi-214, and Po-214), which have a collective half-life of approximately 30 minutes. Known collectively as radon daughters, they decay to lead 210, which has a half life of 22 years. Because there are small amounts of radium in all rocks and soils and in most building materials, radon is ubiquitous and is constantly being emanated from ground surfaces; when it diffuses into the atmosphere, it is rapidly diluted. Radon levels are enhanced whenever radon is emanated into an enclosed space rather than into the open air; therefore, radon levels in most underground mines are higher than in open air. There are elevated levels of radium in uranium and phosphate ores, so there are naturally enhanced levels of radon and its daughters in such underground mines (NCRP 1984a).

Human Exposure to Radiation From Radon Daughters

When radon in air decays, its daughters, being ionized metal atoms, tend to become attached to the nearest solid object, usually a dust particle. These dust particles and attached ions are inhaled by people breathing the air, and a fraction is deposited within the lungs. From the standpoint of radiation dose to the critical cells, the amount deposited on the tracheobronchial epithelium is important. Because radon daughters decay rapidly, they deliver their radiation before they can be removed by normal lung clearance mechanisms. Particles deposited by inertial forces (impaction) would also be present preferentially at bifurcations. Although alpha, beta, and gamma radiations are emitted by radon daughters, the alpha radiation delivers over 95 percent of the radiation dose to the epithelium. The beta and gamma contribution to dose is therefore generally disregarded (NCRP 1984b).

Exposures to radon daughters are generally measured in working levels (WL) or working level months (WLM). One WL is defined as a concentration of any combination of short-lived radon daughters in air that produces, from complete decay, 1.3 times 10^5 MeV (million electron volts) of alpha energy per liter. A person exposed while working for 1 working month (170 hours) in such an atmosphere would receive an exposure of 1 WLM. The maximum permissible exposure for underground miners is 4 WLM per year, which is approximately equivalent to an average monthly exposure of 0.3 WL for 12 working months per year. In the past, many miners in both

uranium and nonuranium mines received cumulative exposures of between 10 and 10,000 WLM. It is primarily from the study of these groups that our information on the health hazards of radon daughters has come. Although inadequately studied, average levels of radon daughters in homes appear to be close to 0.004 WL in the United States (NCRP 1984a).

Use of the awkward WL is justified on the grounds that exposure to the alpha radiation from radon daughters cannot be readily converted to more universal measures of radiation such as "rad" or "rem." Many attempts to do so have been made, yielding values ranging from 0.1 to 10 rad per WLM. A further problem involves estimating the Quality Factor for the alpha radiation involved. Although use of 20 for this factor is recommended (ICRP 1981), the epidemiologic data indicate that from 10 to 15 may be appropriate (Radford 1984).

Smoking Habits of Exposed Miners

Although information on cigarette usage has not been obtained on all mining groups that have been studied for lung cancer, it has been obtained in many of them (Table 1). Cigarette smoking histories of U.S. uranium miners were obtained between 1950 and 1960, when they were admitted to a prospective study group (Lundin et al. 1971). It was found that white uranium miners in the United States smoked a little more heavily than comparable men in the U.S. population and that Navajo miners were extremely light smokers (Tables 2 and 3) (Archer et al. 1976). Swedish miners have a much lower smoking prevalence than U.S. miners (Cederlof et al. 1975; Radford and Renard 1984).

Risks of Lung Cancer Among Smoking and Nonsmoking Miners

Although the cancerous nature of the fatal lung disease of miners in the Joachimsthal and Schneeberg mining areas of central Europe was not noted until 1879 (Harting and Hesse 1879), the disease had been known for three centuries (Pirchan and Sikl 1932). Lung cancer may have resulted in the death of 40 percent or more of the miners (Arnstein 1913). It is now generally agreed that most of these lung cancer deaths may be attributed to radon daughters—and they were occurring at a high frequency prior to the introduction of cigarettes to Europe.

U.S. Uranium Miners

When the first lung cancer among nonsmoking underground U.S. uranium miners was observed in 1965, there had already been

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TABLE 1.—Epidemiological reports on interaction of smoking and cancer

Study	Group studied	Type of analysis	Cancer site	Results
Saccomanno et al. (1967)	U.S. uranium miners	Case collection	Lung	One cancer among nonsmokers vs. >60 among smokers
Lundin et al. (1969)	U.S. uranium miners	Cohort	Lung	Ten times more lung cancer in smokers than nonsmokers
Lundin et al. (1971)	U.S. uranium miners	Cohort	Lung	
Archer et al. (1973)	U.S. uranium miners	Case–control	Lung	Smoker I-L period shorter; histologic type distribution same in smokers and nonsmokers
Axelson and Sundell (1978)	Swedish lead–zinc miners	Case–control	Lung	Smoker I-L period much shorter
Archer et al. (1976)	U.S. uranium miners	Cohort	Lung	
Dahlgren (1979)	Swedish lead–arsenic–sulfide miners	Case–control	Lung	Smoking not large factor in excess lung cancers
Hornung and Samuels (1981)	U.S. uranium miners	Cohort, Cox regression	Lung	
Gottlieb and Husen (1982)	U.S. Navajo uranium miners	Case collection	Lung	Smoking little role in Navajo lung cancers
Damber and Larsson (1982)	Swedish miners	Case–control	Lung	Smoker I-L period shorter
Edling (1982); Edling and Axelson (1983)	Swedish iron miners	Case–control	Lung	Smoker I-L period shorter
Whittemore and McMillan (1983)	U.S. uranium miners	Nested case–control	Lung	
Radford and Renard (1984)	Swedish iron miners	Cohort	Lung	Smoker I-L periods slightly shorter

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TABLE 1.—Continued

Study	Group studied	Type of analysis	Cancer site	Results
Archer (1985)	U.S. uranium miners	Case–control	Lung	Smoker I-L period significantly shorter
Samet, Kutvirt et al. (1984)	U.S. Navajo uranium miners	Case–control	Lung	Smoking little role in Navajo lung cancers
Hinds et al. (1979)	Hospital patients	Case–control	Larynx	Prior dental x rays
Prentice et al. (1983)	A-bomb survivors	Cohort	Esophagus and lung	

TABLE 2.—Cigarette smoking habits of white U.S. uranium miners at study entry and of U.S. nonminer men

Smoking status	Uranium miners (percent)	Nonminers (percent)
Nonsmokers [1]	28.8	45.4
≤1 pack/day	54.2	39.8
>1 pack/day	16.9	14.8

[1] Includes smokers of pipes or cigars only and ex-smokers.
SOURCE: Adapted from Lundin et al. (1971).

TABLE 3.—Cigarette smoking habits of Navajos in U.S. uranium miner study group, at entry

Packs/day	Percentage smoking at entry	Percentage former smokers	Percentage never smoked
0.00	—	—	62.8
0.01–0.19	15.1	2.3	—
0.2–0.59	14.6	1.7	—
0.6–0.99	0.7	0.000	—
≥1.0	2.7	0.001	—

SOURCE: Adapted from Archer et al. (1976).

nearly 80 lung cancer deaths among cigarette-smoking U.S. uranium miners (Archer 1985). Because approximately one-third of the miners did not smoke cigarettes, the discrepancy was so striking that

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it led some observers to blame cigarette smoking for the entire problem and to conclude that if uranium miners did not smoke, they would rarely develop lung cancer.

A second lung cancer among nonsmoking uranium miners was observed in a mortality analysis of the U.S. uranium miner cohort published in 1969 (Lundin et al. 1969). These two cases represented a fourfold excess of lung cancers (only 0.5 case was expected among nonsmokers)—the same relative risk noted for cigarette smokers (15 expected versus 60 observed). Since the U.S uranium miners were known to smoke at a somewhat higher rate than other U.S. men (Table 2), in an analysis of how much extra cancer could be due to this extra smoking, Lundin and colleagues (1971) concluded that this extra smoking could account for no more than a 50 percent increase; a fivefold to tenfold increase had been observed. The discrepancy between smoker and nonsmoker lung cancer rates suggested an interaction between the two agents.

A later study of white U.S. uranium miners reported that the incidence of lung cancer varied both by cumulative amount of radiation exposure and by the intensity of cigarette smoking (Figure 1) (Archer et al. 1978). The mean exposure of these miners was about 870 WLM. Approximately 780 of the uranium miners in the U.S. study group were Navajo Indians. They had a much lower smoking prevalence than white miners (Table 3), but nevertheless had elevated lung cancer rates (Archer et al. 1976; Gottlieb and Husen 1982; Samet, Kutvirt et al. 1984). Many of those who developed lung cancer had smoked little or not at all (Table 4). Most of the lung cancers were therefore attributed to mining exposure (Samet, Kutvirt et al. 1984).

The role of other factors in the lung cancers of U.S. uranium miners was also studied. The induction-latent (I-L) period (time from start of mining to diagnosis of cancer) was shortened by increased age at the start of mining, by cigarette smoking, and by high exposure rates (Archer 1981). The attributable lung cancer risk tended to decline among miners who had reached the age of 65 and had 25 or more years of latency (Roscoe et al. 1983). An updated analysis of these data, using deaths occurring through 1982 and an adjustment of expected numbers of deaths for smoking habits, indicated that the drop in attributable risk appeared to occur mainly among the smokers, not the nonsmokers (Figure 2) (Roscoe et al., in press).

Because the I-L period is dependent on factors other than cigarette smoking (Archer 1981) and the smoking-related shortening of the I-L period was minimal in miners exposed to low radiation dose rates (Radford 1984), a more detailed case–control study was done of U.S. uranium miners (Archer 1985). There were 35 lung cancer cases among nonsmoking underground uranium miners (defined as smok-
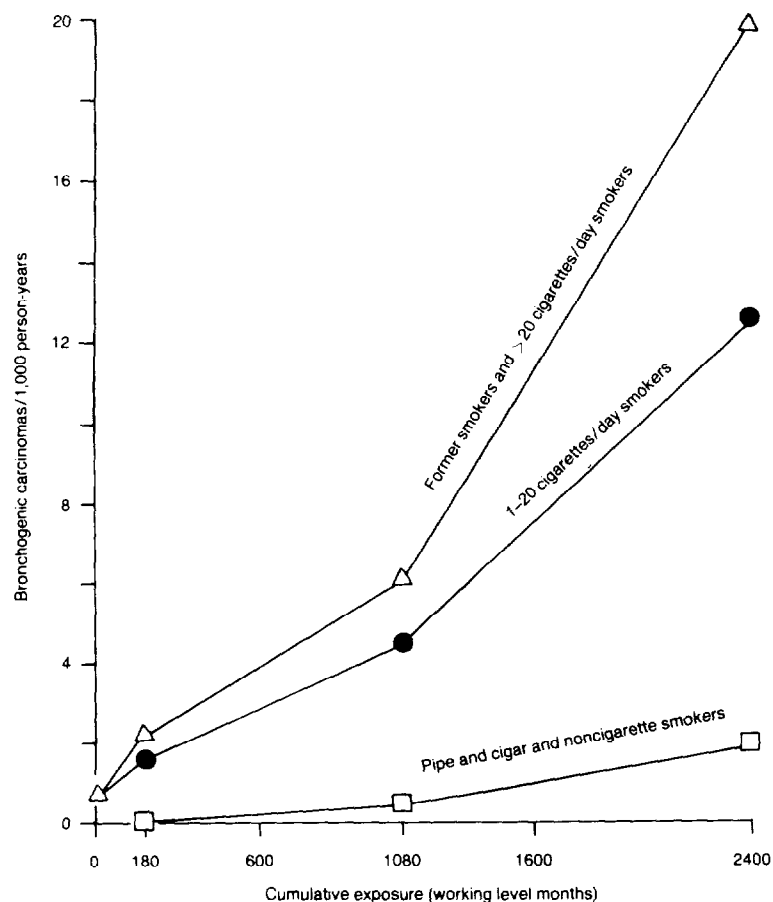
FIGURE 1.—Influence of cigarette smoking and radiation exposure on bronchogenic cancer incidence among U.S. uranium miners

SOURCE: Adapted from Archer et al. (1978).

ing a total of less than four pack-years of cigarettes and not smoking within 10 years of cancer diagnosis) whose lung cancer was diagnosed between January 1964 and January 1984. A few of them had smoked a pipe or cigars occasionally, but not regularly. Because not all of the lung cancer cases were members of the study group, supplemental smoking information was obtained from hospital records and relatives. Two controls were chosen for each case from among 334 smoking U.S. uranium miners. Controls were matched on